LUD 5330.3 DIV (09901357)



**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

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| Applicant(s) | : | Rainer Zimmerman et al. |
| Serial No. | : | 09/265,606 |
| Filed | : | March 10, 1999 |
| For | : | ISOLATED DIMERIC FIBROBLAST ACTIVATION PROTEIN ALPHA, AND USES THEREOF |
| Group Art Unit | : | 1631 |
| Examiner | : | M. Moran |

June 2, 2003

Mail Stop: Appeal Brief – Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

## BRIEF ON APPEAL (37 CFR §1.192)

Sir:

Appellants hereby submit their Brief on Appeal in connection with the above referenced matter. Appeal was noted on April 3, 2003, so this Brief is timely filed.

Three copies of this Brief are submitted, in accordance with 37CFR §1.192(a), as is a check in the amount of $320.00, as prescribed by 37CFR §1.17(c). Should the check, become dislodged, or its amount be incorrect, authorization is given to make appropriate adjustment to Deposit Account 500624.

## 1. REAL PARTY IN INTEREST

The real party in interest is Ludwig Institute for Cancer Research, the assignee of the subject application.

## 2. RELATED APPEALS AND INTERFERENCE'S

Applicants, applicants' legal representatives, and assignee are aware of no other appeals or interference's which will directly affect, be directly affected, or have a bearing on the Board's decision in this appeal.

## 3. STATUS OF CLAIMS

The subject application is a divisional application. As filed, claims 1–15 were presented. Claims 1-4 and 6-15 were cancelled by preliminary amendment, and claims 16-19 were added. In an amendment dated July 1, 2002, these claims were cancelled, and claims 20-26 were presented. Claim 22 was withdrawn from consideration by the examiner, a position which appellants traversed. Claim 22 has NOT been cancelled, but has not been acted upon by the examiner. Claims 20, 21 and 23-26 have been finally rejected, and appellants are appealing from the rejections of all of these claims.

## 4. STATUS OF AMENDMENT

A response to the final rejection, which is dated December 27, 2002, was submitted. No amendments were presented therein. The advisory action of January 24, 2003, indicates that this response was considered.

## 5. SUMMARY OF INVENTION

The invention, as defined by claims 20, 21, and 23-26, relates to isolated proteins which consist of two portions of difference molecules. The first part of the molecule is at least one FAPα catalytic domain. "FAPα" is an acronym for "fibroblast activation protein alpha," as explained at page 2, lines 6-10 of the specification. Page 6, the discussion of figure 3, explains that FAPα has enzymatic activity, i.e., it has extracellular matrix degrading activity.

FAPα shows structured similarity to other molecules with enzymatic activity. This is discussed at page 12 of the specification. Reference is made therein to

> "(T)hree segments corresponding to highly conserved catalytic domains characteristic of serine proteases, such as DPPIV."

See page 12, lines 21-23. The disclosure then goes on to refer to table 2. Table 2 refers to "putative catalytic domains of FAPα, DPPIV and DPPX." It will be seen from these that there is, in fact, a great deal of homology.

Page 21, last paragraph of the specification, describes production of a fusion protein "which comprises the extracellular domains of both FAPα and murine CD8 proteins." This molecule has the same enzymatic activity of FAPα, hence it must contain a catalytic domain.

Written description of the generic invention is provided at Page 22, lines 15-19 of the specification.

## 6. ISSUES

This appeal presents a single issue: did the examiner err in rejection, claims 20, 21 an d 23-26 under 35USC §112, first paragraph, as containing subject matter which was not described in the specification in such a way to convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed inventions. This is characterized by the examiner as a NEW MATTER rejection (paper number 22, page 3). Appellants submit that the examiner did err.

## 7. GROUPING OF CLAIMS

Claims 20, and 24-26 will be grouped together .

Claim 21 will be argued separately.

Claim 23 will be argued separately.

## 8. ARGUMENT

The sole rejection of all of the claims is under 35USC §112. The examiner states this is a new matter rejection, in her final rejection. The examiner's position is essentially that the

disclosure of record does not support the contention that SEQ ID Nos. 4, 6 and 7 correspond to the three sequences set forth at page 12, table 2 of the specification." According to the examiner:

> "(A) teaching that a catalytic domain comprises conserved regions is not a full and complete description of the catalytic domain of FAP$\alpha$."

In their response to the final rejection, appellants made a paper of record, i.e., Niedermeyer, et al, Eur. J. Brockem 254:650-654 (1998) This paper, which is not prior art, was cited to show facts.

One of the facts that it shows is that in the mouse fibroblast activation protein:

> (T)he nucleotides encoding the serine protease consensus motif WGWSYGG all split between two exons."

(Abstract, emphasis added). A serine protease motif is a catalytic domain of human and mouse FAP," and includes WGWSYG.

Comparing this disclosure to the specification, one finds that WGWSYGG is provided in the specification, as a catalytic domain, and as SEQ ID NO: 4.

Niedermeyer goes on to discuss "catalytic triad residues" (page 652, second column), and refers to Ser. 624, Asp 702, and His 734. It is no coincidence that these three residues are all pointed to in Table 2.

The paper goes on to state that "The domains of human and mouse FAP thought to be directly involved in serine protease activity are encoded by exons 21-26." Review of figure 3 shows that WGWSYGG is encoded by exons 22 and 23. Further, the His 734 moiety is found in exon 26.

The fact is, given the evidence submitted during the course of prosecution, and has reiterated herein, there is no reason to doubt that SEQ ID NOS: 4, 6 and 7 do, in fact, constitute catalytic domains. For these reasons, the rejection of claims 20 and 24-26 should be reversed.

With respect to claim 21, the claim requires all of SEQ ID NOS: 4, 6 and 7. These segments are all a part of the extracellular domain Niedermeyer, et al, supra, show this, by way of the statement that these segments are encoded by exons 21-26. As was pointed out, supra,

fusion proteins of the extracellular domain of FAPα and CD8 were active. Indeed, it is submitted that one must assume that any molecule which includes at least SEQ ID NO: 4 must be presumed to have activity. As SEQ ID NO: 4 is required by claim 21, and SEQ ID NO: 4 is considered a catalytic domain, it is believe that claim 21 is free of the rejection. Hence, the rejection should be reversed.

Further, claim 23 requires the presence of a CD8 protein. Such a protein was made, tested, and found active, as discussed, supra. Hence, there is clearly description of the subject matter of claim 23. The rejection of this claim should be reversed as well.

## 9. CONCLUSION

For the foregoing reasons, it is believed that the rejections of claims 20, 21, and 23-26 are improper, and should be revised.

Respectfully submitted,

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